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Studies on Heteropentalenes. II.[1] Cycloaddition of Imidazo[2,1-*b*]thiazoles, Thiazolo[3,2-*a*]benzimidazole, and Imidazo[2,1-*b*]benzothiazole with a Reactive Acetylenic Ester

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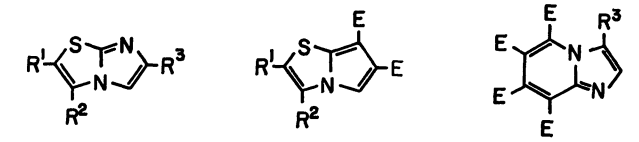
Cycloaddition of imidazo[2,1-*b*]thiazoles with dialkyl acetylenedicarboxylate follows dual courses depending on the polarity of the solvent, affording pyrrolo[2,1-*b*]thiazoles in an aprotic nonpolar solvent, or imidazo[1,2-*a*]-pyridines and imidazo[3,4-*a*]pyridines, together with thiophenes, in an aprotic polar solvent. Thiazolo[3,2-*a*]-benzimidazole and imidazo[2,1-*b*]benzothiazole were also found to react with the acetylenedicarboxylate to give pyrido[1,2-*a*]benzimidazole and pyrrolo[2,1-*a*]benzothiazole, respectively. The reactions would be accounted for in light of the Diels-Alder reaction in an aprotic nonpolar solvent and the 1,4-dipolar cycloaddition in an aprotic polar solvent.

Cycloaddition of nitrogen-heterocycles with acetylenic esters has received attention.[2] Our success in the cycloaddition of azaazulenes with dimethyl acetylenedicarboxylate (DMAD)[3] prompted us to extend the study to aromatic azapentalenes.[4] A number of papers have appeared on the cycloaddition of mesoionic azapentalenes.[5] Attempts to obtain a cycloadduct by reactions of neutral azapentalenes with reactive olefins and/or acetylenes do not seem successful, the reactions of pyrrolo[2,1-*b*]thiazoles with DMAD[6] and those of imidazo[2,1-*b*]thiazoles with maleic anhydride or diethyl azodicarboxylate[7] affording only the Michael adducts. We wish to report on the cycloaddition of imidazo[2,1-*b*]thiazoles and other related 10π-electron bicyclic systems (*e.g.* thiazolo[3,2-*a*]benzimidazole and imidazo[2,1-*b*]benzothiazole) with reactive acetylenic esters.

The reaction of ethyl 3-methyl-6-phenylimidazo[2,1-*b*]thiazole-2-carboxylate (**1a**) with DMAD was carried out under various conditions (Table 1). When the reaction was carried out in boiling acetonitrile, three products, 2-ethyl 6,7-dimethyl 3-methylpyrrolo[2,1-*b*]-thiazole-2,6,7-tricarboxylate (**2a**), tetramethyl 3-phenylimidazo[1,2-*a*]pyridine-5,6,7,8-tetracarboxylate (**3a**), and 5-ethyl 2,3-dimethyl 4-methylthiophene-2,3,5-tricarboxylate (**4**), were isolated in 25, 42, and 41% yields, respectively. The reaction in *N*,*N*-dimethylformamide (DMF) at bp proceeded similarly, but the yield of **2a** in the reaction at room temperature decreased remarkably. When the solvent was replaced by hot xylene, compound **2a** was obtained as the sole product in a better yield than in hot acetonitrile or DMF, benzonitrile being detected in the reaction mixture.

The structures of **2a**, **3a**, and **4** were assigned by means of their spectroscopic data as well as their elemental analyses. The ^{1}H NMR spectrum of **2a** reveals two methyl-singlets at δ 2.75 (3H) and 3.90 (6H), ethyl-signals at δ 1.34 and 4.37, and a singlet at δ 7.58 (1H) assignable to a proton at C-5. The ^{13}C NMR spectrum displays fourteen signals in agreement with the assigned structure. The ^{1}H NMR spectrum of **3a** has a 1H-singlet at δ 7.85 (H-2) together with four methyl-singlets at δ 3.20, 3.90, 3.93, and 4.10, and a phenyl multiplet at δ 7.3—7.5. Of four methyl-singlets, the one resonating at the highest field is assigned to a CO_2Me group at C-5, which should be shielded by a phenyl group at C-3. The ^{1}H NMR spectrum of **4** shows a methyl-singlet at δ 2.49 in addition to signals for ester groups at δ 3.87 (3H, s), 3.93 (3H, s), 1.38 (3H, t, J=7 Hz), and 4.35 (2H, q, J=7 Hz).

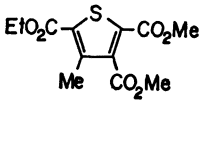
As shown in Table 1, the reaction of **1b** with DMAD in hot xylene proceeded in a similar way to give **2b**, whereas that in hot acetonitrile or DMF afforded tetramethyl 1-phenyl-3-(1-propynylthio)imidazo[3,4-*a*]-pyridine-5,6,7,8-tetracarboxylate (**5**) in addition to **3a**. The structure of **5** was assigned on the basis of the results of elemental analysis as well as its ^{1}H NMR spectrum which has four methyl ester-singlets at δ 3.16, 3.84, 3.91, and 4.07, a methyl-singlet at δ 1.90, and a phenyl multiplet at δ 7.3—7.7. Like **3a**, the singlet at δ 3.16 is assigned to a CO_2Me group at C-8, which should be shielded by a phenyl group at C-1. Resemblance of the UV spectrum of **5** with



1a: R^1=CO_2Et, R^2=Me, R^3=Ph
1b: R^1=H, R^2=Me, R^3=Ph
1c: R^1=CO_2Et, R^2=Me, R^3=t-butyl
1d: R^1=H, R^2=Me, R^3=t-butyl
1e: R^1=R^2=H, R^3=Me

2a: R^1=CO_2Et, R^2=Me, E=CO_2Me
2b: R^1=H, R^2=Me, E=CO_2Me
2f: R^1=E=CO_2Et, R^2=Me
2g: R^1=H, R^2=Me, E=CO_2Et

3a: R^3=Ph, E=CO_2Me
3c: R^3=t-butyl, E=CO_2Me
3e: R^3=Me, E=CO_2Me



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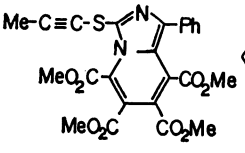

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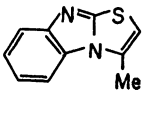

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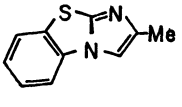

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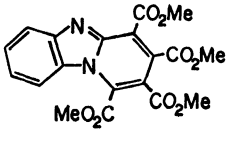

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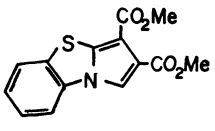

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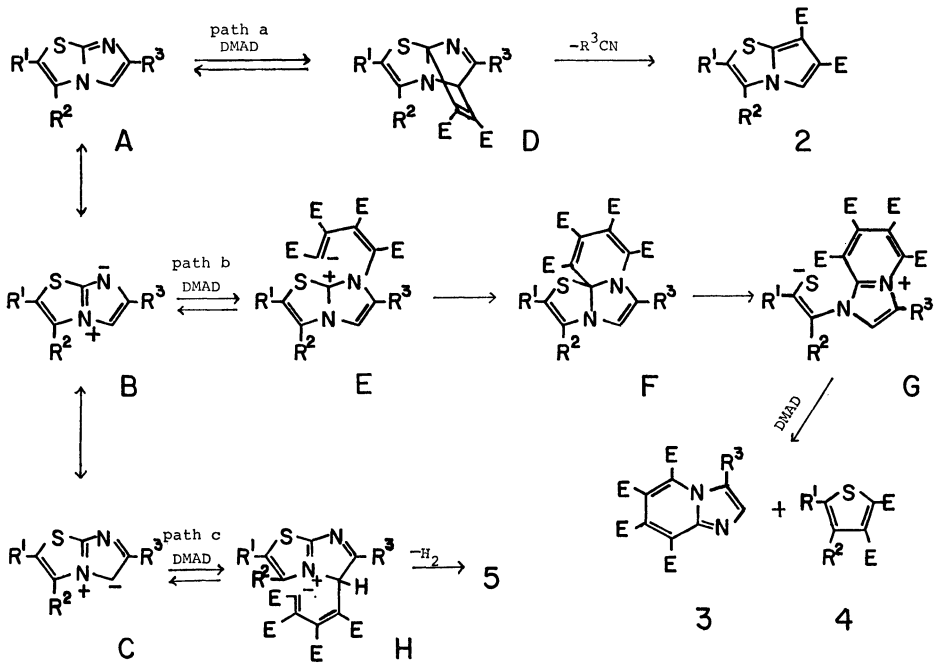
Table 1. Conditions and yields for reactions of **1a—e**, **6**, and **7** with the acetylenic esters

Entry	Substrate	Reagent	Solvent	Temp	Time	Products (%)[a]	Recovery (%)
1	**1a**	DMAD	MeCN	reflux	27 h	**2a** (25), **3a** (42), **4** (41)	**1a** (6)
2	**1a**	DMAD	MeCN	r.t.	11 d	**2a** (16), **3a** (44), **4** (38)	**1a** (68)
3	**1a**	DMAD	DMF	reflux	20 h	**2a** (27), **3a** (56), **4** (26)	**1a** (—)
4	**1a**	DMAD	DMF	r.t.	11 d	**2a** (9), **3a** (65), **4** (61)	**1a** (10)
5	**1a**	DMAD	Xxlene	reflux	27 h	**2a** (63)	**1a** (—)
6	**1a**	DMAD	Xylene	r.t.	27 d	**2a** (42), **3a** (48), **4** (45)	**1a** (82)
7	**1a**	DEAD	Xylene	reflux	27 h	**2f** (63)	**1a** (—)
8	**1b**	DMAD	MeCN	reflux	6 h	**3a** (43), **5** (26)	**1b** (—)
9	**1b**	DMAD	MeCN	r.t.	3 d	**3a** (26)	**1b** (5)
10	**1b**	DMAD	DMF	reflux	2 h	**3a** (42), **5** (30)	**1b** (—)
11	**1b**	DMAD	DMF	r.t.	3 d	**3a** (30)	**1b** (—)
12	**1b**	DMAD	Xylene	reflux	14 h	**2b** (50)	**1b** (—)
13	**1b**	DMAD	Xylene	r.t.	7 d	**2b** (20), **3a** (20)	**1b** (19)
14	**1b**	DEAD	Xylene	reflux	14 h	**2g** (75)	**1b** (—)
15	**1c**	DMAD	MeCN	r.t.	8 d	**3c** (29), **4** (17)	**1c** (25)
16	**1c**	DMAD	Xylene	r.t.	27 d	**2a** (17), **3c** (36)	**1c** (38)
17	**1d**	DMAD	MeCN	reflux	3 h	**3c** (44)	**1d** (—)
18	**1d**	DMAD	MeCN	r.t.	20 h	**3c** (22)	**1d** (5)
19	**1d**	DMAD	Xylene	reflux	4 h	**2b** (76)	**1d** (—)
20	**1d**	DMAD	Xylene	r.t.	7 d	**2b** (12), **3c** (15)	**1d** (32)
21	**1e**	DMAD	MeCN	r.t.	2 h	**3e** (38), **10**(5)	**1e** (—)
22	**1e**	DMAD	Xylene	r.t.	2 h	**3e** (31), **10**(12)	**1e** (—)
23	**6**	DMAD	MeCN	r.t.	3 h	**8** (24)	**6** (—)
24	**7**	DMAD	Xylene	reflux	5 h	**9** (29), **11** (4), **12**(12)	**7** (—)

a) Yields are based on consumed starting materials.



Scheme 1.

that of **3a** further supports the assigned structure.

Likewise, **1a** and **1b** react with diethyl acetylenedicarboxylate (DEAD) in hot xylene giving **2f** and **2g**, respectively, in good yields.

It appears that elimination of nitrogen- or sulfur-containing moiety from **1** highly depends on the polarity of the solvent. For the sake of clarification, 3-methylthiazolo[3,2-*a*]benzimidazole (**6**) and 2-methylimidazo[2,1-*b*]benzothiazole (**7**), respectively, were allowed to react with DMAD. The reaction of **6** in acetonitrile yielded tetramethylpyrido[1,2-*a*]benzimidazole-1,2,3,4-tetracarboxylate (**8**) with loss of the sulfur-containing moiety, whereas that of **7** in xylene gave dimethyl pyrrolo[2,1-*b*]benzothiazole-2,3-dicarboxylate (**9**) with elimination of acetonitrile and two unidentified 1:4-adducts **11** and **12**.

Plausible mechanisms for the reactions of imidazo[2,1-*b*]thiazole **1** with the reactive acetylenic ester are given in Scheme 1. In an aprotic nonpolar solvent, the reaction proceeds *via* a Diels-Alder addition of the neutral species **A** with the acetylenedicarboxylate followed by the retrogression of the adduct **D** to give **2** (path a). In an aprotic polar solvent, the ionic species **B** undergoes a 1,4-dipolar cycloaddition with DMAD to give intermediates **E, F,** and **G** successively. At the final stage of the reaction, **G** reacts with DMAD to give imidazo[1,2-*a*]pyridine (**3**) together with the thiophene (**4**) (path b). Potts *et al.* also postulated a zwitter ion like **G** for the reaction of thiazolium-*N*-ylides with DMAD to give 1*H*-pyrido[2,1-*c*][1,4]thiazines.[8] However, if R^1 in **1** is hydrogen, the ionic species **C** reacts with DMAD to form an intermediate **H**, from which thioether **5** is produced by loss of H_2 (path c).

In order to confirm the postulate that a bulky substituent at C-6 in the imidazo[2,1-*b*]thiazoles facilitates the isolation of intermediates **D** and **F** (Scheme 1), we examined the reactions of **1c** and **1d** with DMAD in xylene or acetonitrile. However, the products were found to be those formed by the loss of the sulfur- or nitrogen-containing moiety from the intermediates.

The reaction of **1a** with the acetylene is sluggish; over 80% yield of the starting **1a** was recovered even after being allowed to react with DMAD in xylene at room temperature for 27 d. The reaction of 6-methylimidazo[2,1-*b*]thiazole (**1e**) with DMAD in either xylene or acetonitrile was rapid and the solution boiled when DMAD was added to a solution of **1e** to give **3e** and an unidentified 1:4-adduct **10**. The results suggest that an electron-attracting substituent would decrease the electron density of the imidazole ring of **1** and hence its nucleophilic reactivity towards the acetylenedicarboxylate, whereas an electron-donating substituent would enhence its reactivity.

No such Michael-type adducts[6,7] were isolated.

Experimental

Melting points were uncorrected. ^{1}H and ^{13}C NMR spectra were taken with Hitachi R-24B (60 MHz) and Varian FT-80A spectrometers, respectively, for solutions in $CDCl_3$ with TMS as an internal standard. UV spectra were measured for solutions in ethanol and IR spectra for Nujol mulls. Kieselgel 60 was used for chromatography. Yields are based on the consumed starting materials. Imidazo[2,1-*b*]thiazoles (**1b** and **1e**),[9,10] thiazolo[3,2-*a*]benzimidazole (**6**),[9] and imidazo[2,1-*b*]benzothiazole (**7**)[9] were prepared as reported.

*Synthesis of Ethyl 3-Methyl-6-phenylimidazo[2,1-*b*]thiazole-2-carboxylate (**1a**).* A stirred mixture of ethyl 2-amino-4-methylthiazole-5-carboxylate[11] (10 g) and α-bromoacetophenone (10.6 g) in 1-butanol (40 ml) was heated under reflux for 3 h and cooled in an ice bath. Ethyl 3-methyl-6-phenylimidazo[2,1-*b*]thiazole-2-carboxylate hydrobromide (8.3 g, 40%) precipitated was recrystallized from ethanol as colorless prisms, mp 199—200 °C. A mixture of the salt (5 g) in water (150 ml) was heated under reflux for 3 h, free base precipitated on cooling, being filtered off and dried (2.3 g, 62%). Recrystallization from ethanol gave **1a** [colorless needles, mp 143—144 °C, UV_{max} 257^{sh} (log ε 4.37), 265 (4.38), 280 (4.38), 287 (4.38), 294^{sh} (4.36); IR 1690 cm^{-1} (ester C=O); ^{1}H NMR δ=1.38 (3H, t, *J*=7 Hz, CH_3), 2.72 (3H, s, CH_3), 4.33 (2H, q, *J*=7 Hz, OCH_2), 7.3—7.5 (3H, m, phenyl), 7.55 (1H, s, H-5), 7.7—7.9 (2H, m, phenyl). Found: C, 62.89; H, 4.97; N, 9.81; S, 11.08%. Calcd for $C_{15}H_{14}N_2O_2S$: C, 62.97; H, 4.93; N, 9.78; S, 11.20%].

*Synthesis of Ethyl 6-t-Butyl-3-methylimidazo[2,1-b]thiazole-2-carboxylate (**1c**).* Ethyl 6-*t*-butyl-3-methylimidazo[2,1-*b*]-thiazole hydrobromide was prepared in 78% yield in the same way as for **1a** from ethyl 2-amino-4-methylthiazole-5-carboxylate (17.5 g), 1-bromo-3,3-dimethyl-2-butanone[12] (16.1 g), and 1-butanol (70 ml) and recrystallized from ethanol as colorless prisms, mp 202—203.5 °C. This salt (3.2 g) was added to a sodium ethoxide solution prepared from Na (0.4 g) and abs ethanol (30 ml). The mixture was heated under reflux for 3 h and evaporated to dryness under reduced pressure, the residue being dissolved in water. Extraction with ether and evaporation of the dried (Na_2SO_4) extracts gave **1c** [1.78 g, 73%, colorless prisms (from ligroine), mp 92—93 °C. UV_{max} 274 nm (log ε 4.18); IR 1680 cm^{-1} (ester C=O); ^{1}H NMR δ=1.36 (9H, s, *t*-butyl), 1.38 (3H, t, *J*=7 Hz, CH_3), 2.73 (3H, s, CH_3), 4.33 (2H, q, *J*=7 Hz, OCH_2), 7.10 (1H, s, H-5). Found: C, 58.87; H, 6.76; N, 10.42; S, 12.29%. Calcd for $C_{13}H_{18}N_2O_2S$: C, 58.62; H, 6.81; N, 10.52; S, 12.04%].

*Synthesis of 6-t-Butyl-3-methylimidazo[2,1-b]thiazole (**1d**).* 6-*t*-Butyl-3-methylimidazo[2,1-*b*]thiazole hydrobromide was prepared in 83% yield in the same way as for **1a** from 2-amino-4-methylthiazole (15.8 g), 1-bromo-3,3-dimethyl-2-butanone (24.7 g) and 1-butanol (70 ml), and recrystallized from ethanol as colorless prisms, mp 242—243 °C. A mixture of this salt (5 g), NaOH (1 g), and ethanol (30 ml) was heated under reflux for 1 h and evaporated to dryness under reduced pressure. The residue was dissolved in water and extracted with ether. Evaporation of the dried (Na_2SO_4) extracts left **1d** [2.8 g, 79%, colorless prisms (from petroleum ether), mp 83—85 °C, UV_{max} 245 nm (log ε 3.80); ^{1}H NMR δ=1.34 (9H, s, *t*-butyl), 2.32 (3H, d, *J*=1 Hz, CH_3), 6.28 (1H, q, *J*=1 Hz, H-2), 7.04 (1H, s, H-5). Found: C, 62.02; H, 7.28; N, 14.38; S, 16.49%. Calcd for $C_{10}H_{14}N_2S$: C, 61.82; H, 7.26; N, 14.42; S, 16.50%].

*Reaction of **1a** with DMAD.* A mixture of **1a** (1.00 g), DMAD (2.48 g), and the solvent (50 ml) was allowed to react and then evaporated to dryness under reduced pressure. Chromatography of the residue with benzene and benzene–chloroform (1:1) eluted benzonitrile [IR (neat) 2200 (CN) and 700 cm^{-1} (phenyl)], compounds **4**, **1a**, **2a**, and **3a**, successively. The conditions and yields for reactions of **1a—e**, **6**, and **7** with acetylenic esters are given in Table 1.

2a: Colorless needles (from ethanol), mp 166.5—167 °C, UV_{max} 226 nm (log ε 4.34), 257^{sh} (4.43), 265 (4.48), 292 (3.82), 316^{sh} (3.58); IR 1730, 1705, and 1655 cm^{-1} (ester (C=O); ^{1}H NMR δ=1.34 (3H, t, *J*=7 Hz, CH_3), 2.75 (3H, s, CH_3), 3.90 (6H, s, 2×OCH_3), 4.37 (2H, q, *J*=7 Hz, OCH_2), 7.58 (1H, s, H-5). ^{13}C NMR δ=12.1 (q, CH_3), 14.2 (q, CH_3), 51.6 (q, OCH_3), 52.0 (q, OCH_3), 61.9 (t, OCH_2), 104.5 (s, C-7), 116.3 (d, C-5), 118.4 (s, C-6), 122.1 (s, C-2), 137.3 (s, C-3), 139.2 (s, C-7a), 161.7 (s, C=O), 162.7 (s, C=O), 163.4 (s, C=O). Found: C, 51.56; H, 4.73; N, 4.17; S, 10.09%. Calcd for $C_{14}H_{15}NO_6S$: C, 51.68; H, 4.65; N, 4.31; S, 9.85%.

3a: Yellow needles (from ethanol), mp 152—153 °C, UV_{max} 261 nm (log ε 4.41), 300^{sh} (3.69), 357 (3.53); IR 1740, 1730, and 1715 cm^{-1} (ester C=O); ^{1}H NMR δ=3.20 (3H, s, OCH_3), 3.90 (3H, s, OCH_3), 3.93 (3H, s, OCH_3), 4.10 (3H, s, OCH_3), 7.3—7.5 (5H, m, phenyl), 7.85 (1H, s, H-2). Found: C, 58.98; H, 4.56; N, 6.78%. Calcd for $C_{21}H_{18}N_2O_8$: C, 59.15;

H, 4.26; N, 6.57%.

4: Colorless needles (from ethanol), mp 67—68 °C, UV_{max} 275 nm (log ε 4.27); IR 1740, 1720, and 1705 cm^{-1} (ester C=O); ^1H NMR δ=1.38 (3H, t, *J*=7 Hz, CH_3), 2.49 (3H, s, CH_3), 3.87 (3H, s, OCH_3), 4.35 (2H, q, *J*=7 Hz, OCH_2). Found: C, 50.53; H, 4.99; S, 11.03%. Calcd for $C_{12}H_{14}O_6S$: C, 50.34; H, 4.93; S, 11.20%.

*Reaction of **1a** with DEAD.* A mixture of **1a** (0.70 g) and DEAD (1.66 g) in xylene (30 ml) was heated under reflux for 27 h, and worked up as above to give **2f**.

2f: Colorless needles (from ligroine), mp 109—110 °C, UV_{max} 226 nm (log ε 4.19), 257^{sh} (4.42), 265 (4.49), 292^{sh} (3.92), 316 (3.67); IR 1725, 1710, and 1650 cm^{-1} (ester C=O); ^1H NMR δ=1.40 (9H, t, *J*=7 Hz, 3×CH_3), 2.75 (3H, s, CH_3), 4.37 (6H, q, *J*=7 Hz, 3×OCH_2), 7.58 (1H, s, H-5). Found: C, 54.54; H, 5.68; N, 4.08; S, 9.27%. Calcd for $C_{16}H_{19}NO_6S$: C, 54.38; H, 5.42; N, 3.96; S, 9.07%.

*Reaction of **1b** with DMAD.* A mixture of **1b** (1.00 g), DMAD (3.32 g), and the solvent (30 ml) was allowed to react and then worked up as for **1a**. Compound **1b**, **5**, and **2b** were eluted successively.

2b: Colorless needles (from ligroine–benzene), mp 148—149 °C, UV_{max} 225 nm (log ε 4.28), 242 (4.29), 290 (4.08); IR 1725 and 1705 cm^{-1} (ester C=O); ^1H NMR δ=2.43 (3H, d, *J*=0.5 Hz, CH_3), 3.93 (6H, s, 2×OCH_3), 6.62 (1H, q, *J*=0.5 Hz, H-2), 7.62 (1H, s, H-5). Found: C, 51.99; H, 4.37; N, 5.50; S, 12.48%. Calcd for $C_{11}H_{11}NO_4S$: C, 52.16; H, 4.38; N, 5.53; S, 12.66%.

5: Yellow needles (from ethanol), mp 186—187 °C, UV_{max} 255 nm (log ε 4.14), 297^{sh} (3.74), 373 (3.59); IR 1735 and 1710 cm^{-1} (ester C=O); ^1H NMR δ=1.90 (3H, s, CH_3), 3.16 (3H, s, OCH_3), 3.84 (3H, s, OCH_3), 3.91 (3H, s, OCH_3), 4.07 (3H, s, OCH_3), 7.3—7.7 (5H, m, phenyl). Found: C, 58.14; H, 4.16; N, 5.35; S, 6.14%. Calcd for $C_{24}H_{20}N_2O_8S$: C, 58.06; H, 4.06; N, 5.46; S, 6.46%.

*Reaction of **1b** with DEAD.* A mixture of **1b** (1.00 g) and DEAD (3.18 g) in xylene (30 ml) was heated under reflux for 14 h, and then worked up as for **1a** to give **2g**.

2g: Colorless prisms (from ethanol), mp 114—115 °C, UV_{max} 225 nm (log ε 4.18), 235 (4.18), 243 (4.18), 291 (3.96); IR 1720 and 1695 cm^{-1} (ester C=O); ^1H NMR δ=1.39 (6H, t, *J*=7 Hz, 2×CH_3), 2.40 (3H, d, *J*=1 Hz, CH_3), 4.34 (4H, q, *J*=7 Hz, 2×OCH_2), 6.52 (1H, q, *J*=1 Hz, H-2), 7.52 (1H, s, H-5). Found: C, 55.53; H, 5.33; N, 4.85; S, 11.34%. Calcd for $C_{13}H_{15}NO_4S$: 55.50; H, 5.37; N, 4.98; S, 11.40%.

*Reaction of **1c** with DMAD.* A mixture of **1c** (0.90 g), DMAD (2.40 g), and the solvent (50 ml) was allowed to react and then worked up as for **1a** to give compounds **4**, **1c**, **2a**, and **3c** successively.

3c: Yellow needles (from ethanol), mp 119—120 °C, UV_{max} 261 nm (log ε 4.34), 302 (3.52), 358 (3.60); IR 1735 and 1710 cm^{-1} (ester C=O); ^1H NMR δ=1.47 (9H, s, *t*-butyl), 3.90 (6H, s, 2×OCH_3), 3.93 (3H, s, OCH_3), 4.05 (3H, s, OCH_3), 7.82 (1H, s, H-2). Found: C, 56.24; H, 5.47; N, 6.71%. Calcd for $C_{19}H_{22}N_2O_8$: C, 56.15; H, 5.46; N, 6.89%.

*Reaction of **1d** with DMAD.* A mixture of **1d** (1.00 g), DMAD (3.60 g), and the solvent (30 ml) was allowed to react and then worked up as for **1a** to give compounds **2b** and **3c** successively.

*Reaction of **1e** with DMAD.* A mixture of **1e** (1.00 g), DMAD (4.12 g), and the solvent (30 ml) was allowed to react and then worked up to give **3e** as a yellow oil, identified as a picrate, and an unidentified 1:4-adduct **10**.

3e: Picrate of **3e**, yellow prisms (from ethanol), mp 153—154 °C, UV_{max} 255 nm (log ε 4.56), 315^{sh} (4.03), 354 (4.31); IR 3350 (OH) and 1740 cm^{-1} (ester C=O); ^1H NMR (DMSO-d_6) δ=1.07 (3H, t, *J*=7 Hz, CH_3), 2.42 (3H, d, *J*=0.5 Hz, CH_3), 3.45 (2H, q, OCH_2), 3.87 (6H, s, 2×OCH_3), 3.95 (3H, s, OCH_3), 4.03 (3H, s, OCH_3), 7.13 (1H, bs, OH), 7.45 (1H, q, *J*=0.5 Hz, H-2), 7.95 (1H, bs, OH), 8.53 (2H, s, phenyl). Found: C, 45.44; H, 3.84; N, 10.85%. Calcd for $C_{22}H_{20}N_5O_{15}\cdot C_2H_5OH$: C, 45.08; H, 3.94; N, 10.95%.

10: Yellow prisms (from ethanol), mp 235—236 °C, UV_{max} 298 nm (log ε 4.20), 420 (4.06); IR 1730, 1705, and 1685 cm^{-1} (ester C=O); ^1H NMR δ=1.57 (3H, s), 3.62 (3H, s), 3.67 (3H, s), 3.75 (6H, s), 3.76 (3H, s), 3.83 (3H, s), 3.85 (3H, s), 3.88 (3H, s), 5.26 (1H, d, *J*=8 Hz), 6.43 (1H, s), 6.45 (1H, d, *J*=8 Hz). Found: C, 50.89; H, 4.40; N, 3.86; S, 4.50%. Calcd for $C_{30}H_{30}N_2O_{16}S$: C, 50.99; H, 4.28; N, 3.96; S, 4.54%.

*Reaction of **6** with DMAD.* A mixture of **6** (1.00 g) and DMAD (3.87 g) in acetonitrile (30 ml) was left to stand at room temperature for 3 h, and worked up as described for **1a** to give **8** (0.51 g).

8: Yellow needles (from ligroine–benzene), mp 146—147 °C, UV_{max} 277 nm (log ε 4.60), 285^{sh} (4.56), 326 (3.68), 375 (3.45); IR 1740 and 1730 cm^{-1} (ester C=O); ^1H NMR δ=3.90 (3H, s, OCH_3), 3.92 (3H, s, OCH_3), 4.08 (3H, s, OCH_3), 4.20 (3H, s, OCH_3), 7.3—7.8 (3H, m, H-7,8,9), 8.07 (1H, dm, *J*=8 Hz, H-6). Found: C, 57.12; H, 3.97; N, 6.92%. Calcd for $C_{19}H_{16}N_2O_8$: C, 57.00; H, 4.03; N, 7.00%.

*Reaction of **7** with DMAD.* A mixture of **7** (0.94 g) and DMAD (2.13 g) in xylene (30 ml) was heated under reflux for 5 h, and worked up as described for **1a** to give **9** (0.213 g) and two unidentified 1:4-adducts **11** (0.138 g) and **12** (0.47 g).

9: Colorless needles (from ethanol), mp 147—149 °C, UV_{max} 241 nm (log ε 4.62), 268^{sh} (4.13), 288 (4.13); IR 1740 and 1710 cm^{-1} (ester C=O); ^1H NMR δ=3.95 (6H, s, 2×OCH_3), 7.2—7.8 (4H, m, H-5,6,7,8), 7.98 (1H, s, H-1). Found: C, 58.07; H, 3.98; N, 4.98; S, 11.38%. Calcd for $C_{14}H_{11}NO_4S$: C, 58.12; H, 3.83; N, 4.84; S, 11.08%.

11: Yellow prisms (from ethanol), mp 234—235 °C, UV_{max} 291 nm (log ε 4.37), 414 (4.28); IR 1750, 1735, and 1700 cm^{-1} (ester C=O); ^1H NMR δ=1.72 (3H, s), 2.92 (3H, s), 3.48 (3H, s), 3.67 (3H, s), 3.68 (3H, s), 3.72 (3H, s), 3.78 (3H, s), 3.83 (3H, s), 3.86 (3H, s), 5.05 (1H, s), 7.2—7.6 (4H, m). Found: C, 53.98; H, 4.45; N, 3.50; S, 4.51%. Calcd for $C_{34}H_{32}N_2O_{16}S$: C, 53.96; H, 4.27; N, 3.70; S, 4.24%.

12: Orange needles (from ethanol), mp 163—165 °C, UV_{max} 265 nm (log ε 4.15), 435 (3.80); IR 1735, 1725, and 1670 cm^{-1} (ester C=O); ^1H NMR δ=1.67 (3H, s), 3.37 (3H, s), 3.50 (6H, s), 3.61 (3H, s), 3.71 (3H, s), 3.80 (3H, s), 3.84 (3H, s), 3.88 (3H, s), 5.95 (1H, s), 7.05—8.0 (4H, m). Found: C, 54.02; H, 4.41; N, 3.33; S, 4.35%. Calcd for $C_{34}H_{32}N_2O_{16}S$: C, 53.96; H, 4.27; N, 3.70; S, 4.24%.

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